Reappraising the clinical impact of mepolizumab

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We read with interest the recent MUSCA trial from Chupp and colleagues[1] which concluded that mepolizumab was associated with significant improvements in health related quality of life (QOL) in patients with severe eosinophilic asthma (SEA) and therefore support its use as a favourable add-on treatment option to standard of care. Unfortunately there are several issues with the minimum clinically important difference (MCID) for the presented data which make this conclusion untenable.

The primary outcome of the St George's Respiratory Questionnaire (SGRQ) was specially designed for use in COPD rather than asthma[2], whereas the disease specific asthma quality of life questionnaire (AQLQ) is more appropriate to patients with asthma[3]. At end point after 24 weeks the mean change in SGRQ total score was -7·7 which although statistically significant only amounted to a "slightly effective" change (MCID >-4·0), but less than the MCID thresholds for a "moderately effective" change (>-8·0) or a "very effective" change (>-12)[4]. There appeared to be no difference in effects of mepolizumab on SGRQ according to low or high blood eosinophil counts, in turn suggesting that they chose the wrong QOL instrument for patients with SEA.

Moreover the 120 ml mean improvement in FEV1 was less than the MCID of 230ml[5], while the mean change in asthma control questionnaire (ACQ) of -0·4 was also less than the MCID of -0·5[3]. For comparison in a study with dupilumab after 12 weeks there were mean improvements in ACQ (-0·73) and FEV1 (0·27) which both exceeded their respective MCID's[6].

These findings all point to a statistically significant but clinically meaningless impact on quality of life, lung function and asthma control. Prescribers therefore need to be aware when following SEA patients with mepolizumab that its effects in reducing exacerbations may be disconnected from these other important clinical outcomes.

It is also worth noting that the MUSCA trial excluded patients who smoked, which means the findings may not be pertinent to more deprived areas where smoking is highly prevalent among asthma patients. Finally their cohort exhibited a mean reversibility to salbutamol of 21%, which in our experience is unusually high for patients with severe asthma. Hence we would have reservations that these findings from a highly selective group may not be generalizable to patients with SEA in a more real life setting.

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